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| 09/674,815 | 12/07/2000 | Akira Aomatsu | 5836-01-MJA | 5030 |

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| ART UNIT | PAPER NUMBER |
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Please find below and/or attached an Office communication concerning this application or proceeding.

9-2009

| Office Action Summary | Application No. 09/674,815 | Applicant(s) AOMATSU, AKIRA | |
|---|---|---|---|
| | Examiner Brian S Kwon | Art Unit 1614 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *02 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-9 and 18-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 18-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

### *RCE Application*

1. Acknowledgment is made of applicant's filing of US Application No. 09/674815 as a Request For Continued Examination (RCE).

### *Status of Application*

2. By Amendment filed December 02, 2002, claim 1 has been amended and claims 23-24 have been newly added. Claims 1-9 and 18-24 are currently pending for prosecution on the merits.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-9 and 23-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification fails to provide a support for a negative limitation such as "when R2 is a phenyl or naphthyl group which is mono-, di- or tri-substituted with a halogen atom, the α-amino acid is not glycine; and provided that when the 4-amino-3-substituted-butanoic acid derivative is gabapentin, the α-amino is not methyl-D-aspartic acid" in claim 1.

The specification discloses gabapentin, pregabalin, baclofen as examples of a 3-amino-4-butanoic acid derivative. Further, methyl-D-aspartic acid and glycine are disclosed as a possible α-amino acid (for example, page 38, line1 and lines 23-26). The specification discloses the use of glycine, L-alanine, D-alanine, DL-alanine, Na glutamate and Na aspartate alone or in any combination thereof as a preferred α-amino acid when a masking effect against a bitter taste peculiar to a 4-amino-3-substituted-butanoic acid derivative is desired to achieve (page 40, lines 8-13 and page 41, lines 22-26); and the use of L-leucine, L-isoleucine, L-valine, D-leucine, D-isoleucine, D-valine, DL-leucine, Dl-isoleucine or DL-valine as a preferred α-amino acid when a lubricant effect is desired to achieve (page 41, lines 26-28 and page 42, lines 3-5). As the specific embodiment of the instant invention, Examples identifies the use of L-valine in gabapentin preparation (Example 1); glycine in gabapentin preparation (Examples 2, 4, 7); the combination of glycine and DL-alanine in gabapentin preparation (Example 3); L-isoleucine in gabapentin preparation (Examples 5-6); glycine or L-valine in pregabalin preparation (Example 8); L-leucine in pregabalin preparation (Example 9); glycine in balcofen preparation (Example 10);and L-isoleucine in baclofen preparation (Example 11).

A worker skilled in the art reading the instant application would have understood that various α-amino acids recited in the specification (page 38, line 1 thru page 39, line 2) alone or in combination could be useful in stabilizing 4-amino-3-substituted-butanoic acid derivatives, namely gabapentin, pregabalin or baclofen. Further, the worker skilled in the art would have understood that glycine, L-alanine, D-alanine, DL-alanine, Na glutamate and Na aspartate alone or in any combination thereof could be utilized when a masking effect against a bitter taste peculiar to a 4-amino-3-substituted-butanoic acid derivative is desired to achieve (page 40, lines

8-13 and page 41, lines 22-26), and that L-leucine, L-isoleucine, L-valine, D-leucine, D-isoleucine, D-valine, DL-leucine, Dl-isoleucine or DL-valine would be utilized when a lubricant effect is desired to achieve.

However, the skilled worker had no way of obtaining that when R2 is a phenyl or naphthyl group which is mono-, di- or tri-substituted with a halogen atom, the α-amino acid is not glycine, and provided that when the 4-amino-3-substituted-butanoic acid derivative is gabapentin, the α-amino is not methyl-D-aspartic acid. Especially in view of Example 10 showing the use of glycine in preparing baclofen composition, it is clear that applicants were never contemplated of such negative limitation "R2 is a phenyl or naphthyl group which is mono-, di- or tri-substituted with a halogen atom, the α-amino acid is not glycine". Further, it appears in view of the instant specification filed originally that applicants were never contemplated of "when the 4-amino-3-substituted-butanoic acid derivative is gabapentin, the α-amino is not methyl-D-aspartic acid".

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 18 and 20 are rejected under 35 USC 102(b) as being anticipated by Woodruff (US 5084479).

Woodruff discloses a solution comprising N-methyl-D-aspartic acid and gabapentin (column 8, line 5).

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1-9, 19, 21-22 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seiler et al. (Gen. Pharmac. Vol. 15, No. 4, pp. 367-369, 1984) in view of Costa et al. (US 5248678).

Seiler teaches or suggests the synergistic anticonvulsant effects of a GABA agonist and alpha-amino acid such as glycine. The reference discloses muscimol as the specific example of a GABA agonist.

Costa teaches or suggests the use of gabapentin, baclofen, vigabatrin and muscimol as GABA agonists.

The teaching of Seiler differs from the claimed invention (i) in the combination use of gabapentin and glycine in a composition; (ii) the specific amount of alpha-amino acid (e.g., glycine) in said composition; (iii) the specific dosage formulation, for example liquid or solid preparation. To incorporate such teaching into the teaching of Seiler, would have been obvious in view of Costa who teaches or suggests the use of gabapentin as a GABA agonist.

One having ordinary skill in the art would have expected that gabapentin would have a similar property as muscimol due to its GABA agonist activity. Further, one having ordinary skill in the art would have been motivated to make such modification such that the combination of gabapentin and glycine in a composition would provide synergistic anticonvulsant effect.

In addition, optimization of amounts of known active and/or inactive ingredients in a composition or determination of the specific delivery dosage form having optimum therapeutic index is well considered within the skill of the artisan, absent evidence to the contrary.

6. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Seiler et al. (Gen. Pharmac. Vol. 15, No. 4, pp. 367-369, 1984) in view of Costa et al. (US 5248678).

The modified teaching of Seiler includes all that is recited in claim 23 except the use of glycine derivatives such as phenylglycine, hydroxyphenylglycine or dihydroxyphenylglycine. However, one having ordinary skill in the art would have the reasonable expectation that glycine derivatives such as phenylglycine, hydroxyphenylglycine or dihydroxyphenylglycine would not

significantly alter the analogous properties of the compound of the reference due to close structural similarity of the compounds.

***Response to Arguments***

7. Applicant's arguments filed December 2, 2002 have been fully considered but they are not persuasive.

Applicants argument takes position that the specification as filed reasonably conveys to one skilled in the art that applicants had possession of such negative limitation "when 3-amino-4-butanoic acid derivative is gabapentin, the alpha-amino acid is not methyl-D-aspartic acid". Applicants allege that since methyl-D-aspartic acid is never the alpha-amino acid when 3-amino-4-butanoic acid is gabapentin in the eight working examples (as well as the fact that specification identifies gabapentin as one example of a 3-amino-4-butanoic acid derivative along with methyl-D-aspartic acid as a possible alpha-amino acid), the specification as a whole provides a support for such negative limitation. See page 23, para. 4 thru page 24, para. 2 of Remarks filed December 02, 2002.

The examiner strongly disagrees. As the Examiner discussed in preceding 35 U.S.C. 112, first paragraph, new matter rejection, the skilled worker had no way of obtaining that when the 4-amino-3-substituted-butanoic acid derivative is gabapentin, the α-amino is not methyl-D-aspartic acid. Unlike applicants argument, the skilled artisan would have understood from the specification that any of alpha-amino acids (disclosed in page 38, line 1 thru page 39, line 25 of the specification) could be mixed with any of 4-amino-3-substituted-butanoic acid derivative represented by the formula. In other words, the skill artisan would have known in view of the present specification that methyl-D-aspartic acid could be mixed with gabapentin. Clearly,

applicants were never contemplated of "when the 4-amino-3-substituted-butanoic acid derivative is gabapentin, the α-amino is not methyl-D-aspartic acid". In addition, reading the specification (especially Examples 1-8), the skilled artisan would have understood that the specific embodiments shown in Examples are non-limiting examples of the present invention. Further, the skilled artisan would have understood that the specific amino acids (e.g., glycine, L-isoleucine, L-leucine, L-valine) are preferred examples of alpha-amino acids to provide either lubricant effect or masking effect of bitter taste of 4-amino-3-substituted-butanoic acid as well as stabilizing effect. Unlike applicants argument, the skilled artisan would not be possible to the conclusion of such negative provisio.

## Conclusion

8. No Claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (703)308-5377. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax number for this Group is (703) 308-4556.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

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Brian Kwon

**ZOHREH FAY**
**PRIMARY EXAMINER**
**GROUP 1600**